TABLE 1

Anti-TNF Therapy can Effectively Prevent Mortality during Acute DSS-Induced Colitis in Mice

Treatment	No. of survivors/no. tested	% Survival
Untreated	22/42	52
Preimmune	5/10	50
Anti-TNF	10/10	100

TABLE 2

Anti-TNF Therapy can Effectively Prevent Bloody Stools during Acute DSS-Induced Colitis in Mice

Treatment	No. of Hemocult positive/no. tested	% Hemocult positive
Untreated	13/15	87
Preimmune	12/13	92
Anti-TNF	3/14	21

TABLE 3

Anti-TNF Therapy can Effectively Treat Acute DSS-Induced Colitis in Mice

Treatment	No. of survivors/no. tested	% Survival	% Diarrhea
Untreated	8/15	53	87
Preimmune	4/13	31	92
Anti-TNF	13/14	93	21

Figure 1

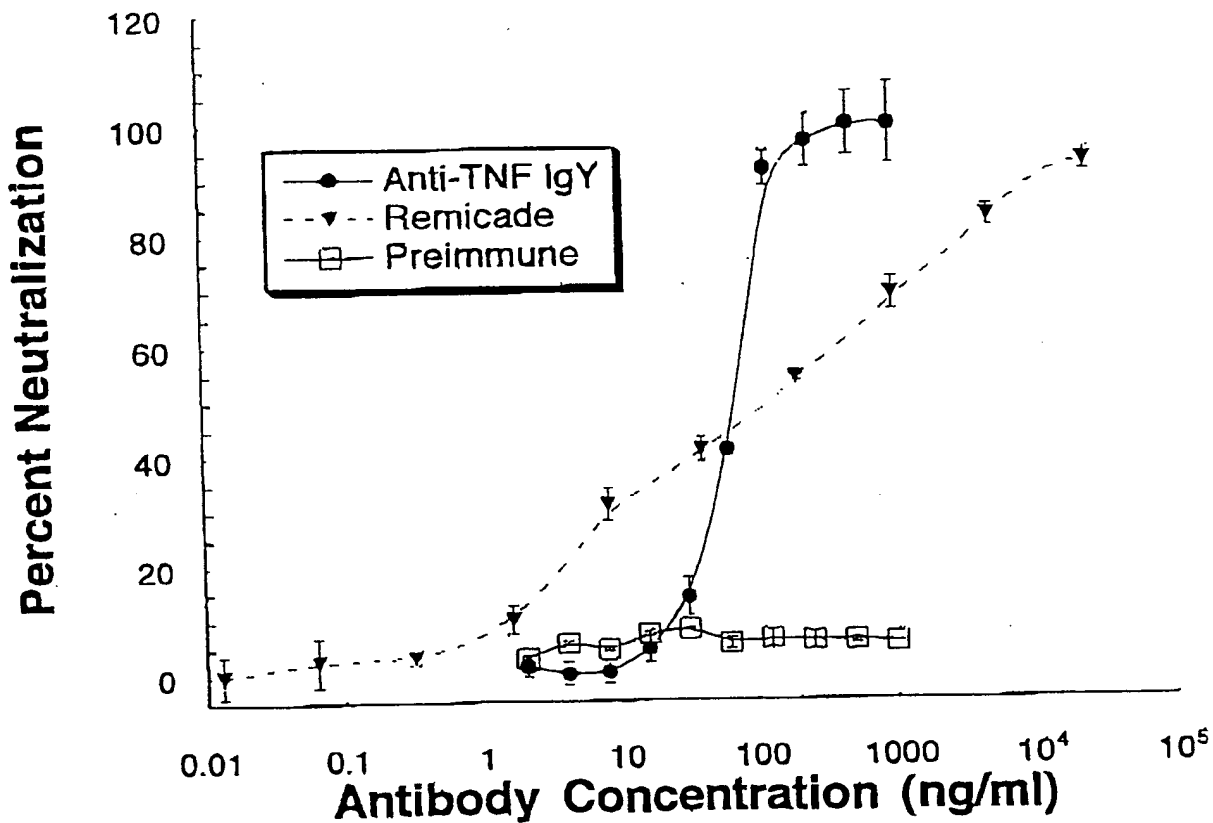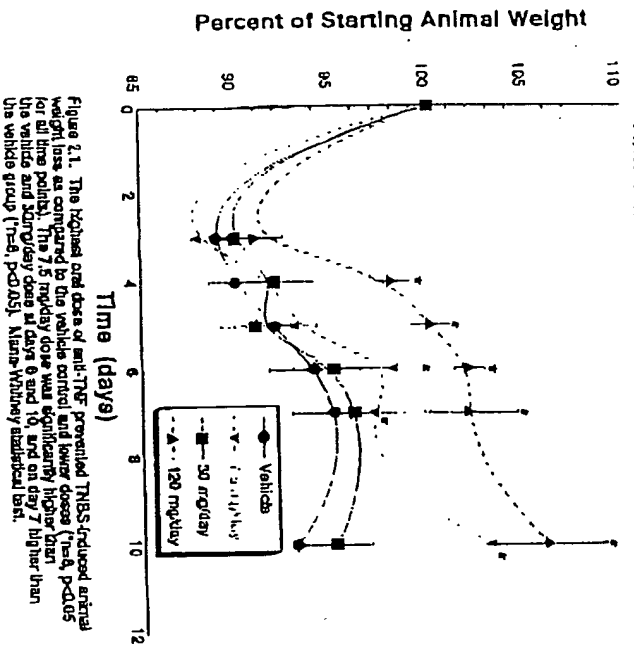## Anti-TNF IgY has Greater Neutralization Activity than Remicade in a Cell-Based Assay

Figure 1.1. The L929 cell based assay shows the greater neutralization ability of anti-TNF IgY as compared to Remicade. The dose of antibody which prevents 50 percent of the cytotoxicity associated with TNF (ND50) is 70 ng/ml for the anti-TNF IgY, and 140 ng/ml for Remicade.
Note: The concentrations graphed for the Remicade antibody represent the total amount of specific antibody, whereas the anti-TNF IgY concentrations represent total IgY concentrations, not specific for TNF.

Figure 2

Treatment of Crohn's Disease by Various Doses of Anti-TNF in the TNBS Animal Model
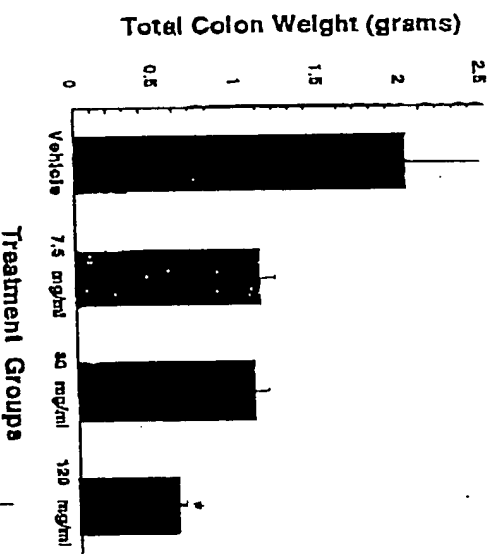
Percent of Starting Animal Weight

Legend:
- ● Vehicle
- ▼ 7.5 mg/day
- ■ 30 mg/day
- ▲ 120 mg/day

Time (days)

Figure 2.1. The highest oral dose of anti-TNF prevented TNBS-induced animal weight loss as compared to the vehicle control and lower doses (*n=8, p<0.05 for all time points). The 7.5 mg/day dose was significantly higher than the vehicle and 30 mg/day dose at days 8 and 10, and on day 7 higher than the vehicle group (*n=8, p<0.05). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Various Doses of Anti-TNF in the TNBS Animal Model

Histology Score

Vehicle — 7.5 mg/day — 30 mg/day — 120 mg/day

Treatment Groups

Figure 2.3. Oral treatment with the highest dose of anti-TNF significantly reduced the histological damage as compared to the vehicle and two other doses (*n=8, p<.0025, p<.0005, and p<.026). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Various Doses of Anti-TNF in the TNBS Animal Model

Total Colon Weight (grams)

Vehicle — 7.5 mg/ml — 30 mg/ml — 120 mg/ml

Treatment Groups

Figure 2.2. Oral treatment with anti-TNF reduced the mean total colon weight at all doses measured. The 120 mg/day dose is statistically significant as compared to the vehicle and lower doses(*n=8, p<.0025, p<.0005, p<.01). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Various Doses of Anti-TNF in the TNBS Animal Model

MPO (unit/gram/min)

Vehicle — 7.5 mg/day — 30 mg/day — 120 mg/day

Treatment Groups

Figure 2.4. Oral administration of 120 mg/day of anti-TNF significantly reduces MPO levels as compared to the vehicle control, as well as the 7.5 mg/day and 30 mg/day doses. (*n=8, p<.0025, p=.005, and p<.005 respectively) Mann-Whitney statistical test.

Figure 3

Treatment of Crohn's Disease by Anti-TNF in the TNBS Animal Model

Total Colon Weight (grams)

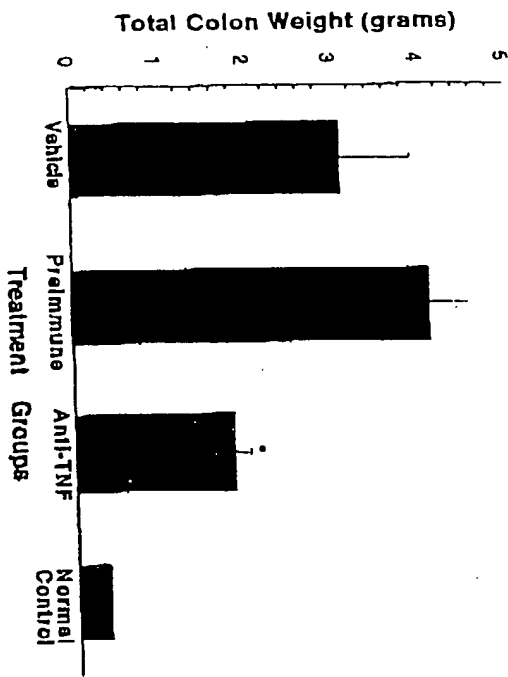Treatment Groups: Vehicle, Preimmune, Anti-TNF, Normal Control

Figure 3.1. Oral delivery of anti-TNF antibodies reduced colonic weight gain associated with TNBS treatment. The anti-TNF reduction was statistically significant as compared to the preimmune treated control (*n=8, p<0.001). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF in the TNBS Animal Model

Histology Score

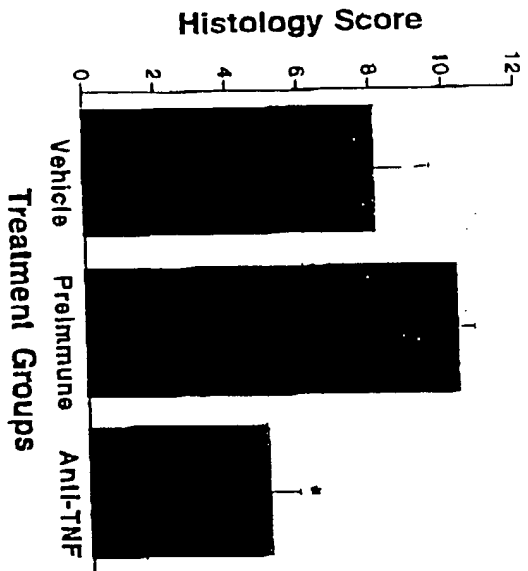Treatment Groups: Vehicle, Preimmune, Anti-TNF

Figure 3.3. Treatment with anti-TNF reduces histological damage as compared to the vehicle and preimmune control animals (*n=7, p<0.05 and p<0.0025 respectively). ... Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF in the TNBS Animal Model

Morphological Damage Score

Treatment Groups: Vehicle, Preimmune, Anti-TNF

Figure 3.2. Oral delivery of anti-TNF reduced histological damage for rats treated with TNBS as compared to vehicle (n=7, *p<0.05) and preimmune controls (n=8, *p<0.001). Normal control was zero. Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF in the TNBS Animal Model

MPO (unti/gram/min)

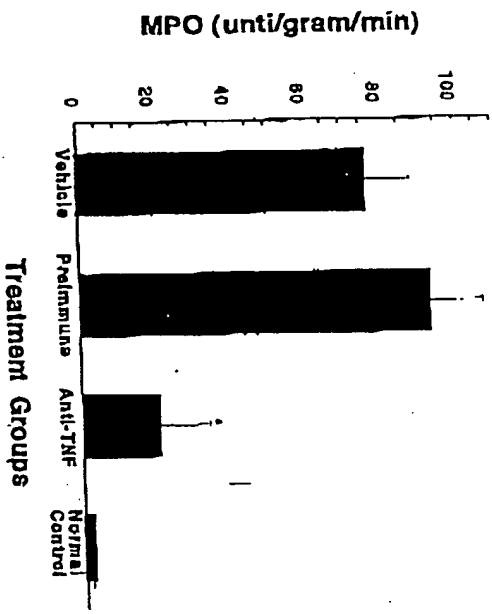Treatment Groups: Vehicle, Preimmune, Anti-TNF, Normal Control

Figure 3.4. Oral delivery of anti-TNF antibodies significantly reduced the levels of tissue myeloperoxidase after rat treatment with TNBS as compared to the preimmune (*n=8, p<0.01) and the vehicle controls (*n=7, p<0.05), Mann-Whitney statistical test.

Figure 4

Treatment of Crohn's Disease by Anti-TNF is more Effective than Sulfasalazine in the TNBS Animal Model

Total Colon Weight (grams)

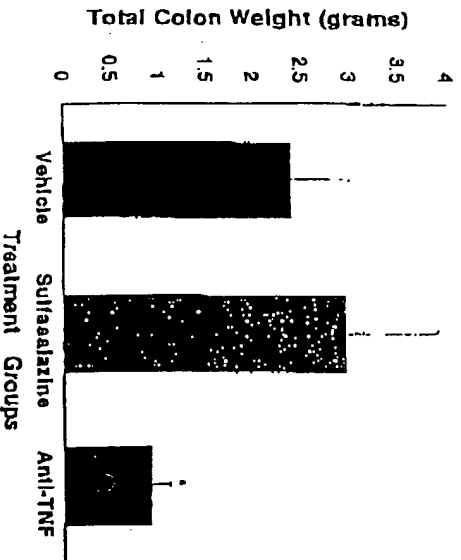Treatment Groups: Vehicle, Sulfasalazine, Anti-TNF

Figure 4.1. Oral administration of anti-TNF antibodies to rats 48 hours post treatment with TNBS significantly decreased disease associated colonic weight gain as compared to vehicle treated animals (*p<0.05). Sulfasalazine saw no improvement over controls. Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Sulfasalazine in the TNBS Animal Model

Mean Histological Score

Treatment Groups: Vehicle, Sulfasalazine, Anti-TNF

Figure 4.3. Treatment with anti-TNF significantly reduces histological damage as compared to the sulfasalazine and vehicle treated controls (n=7, p<0.01 and p<0.001 respectively). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Sulfasalazine in the TNBS Animal Model

Morphological Damage Score

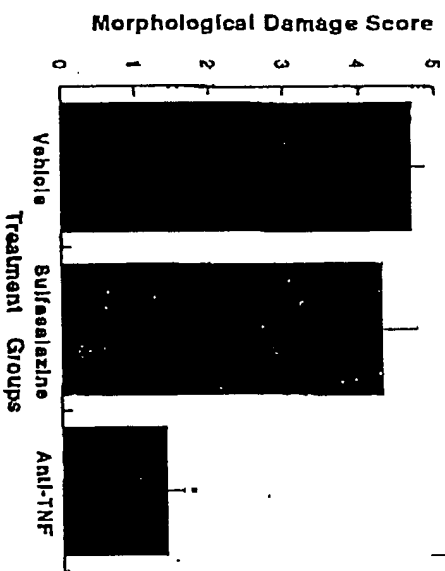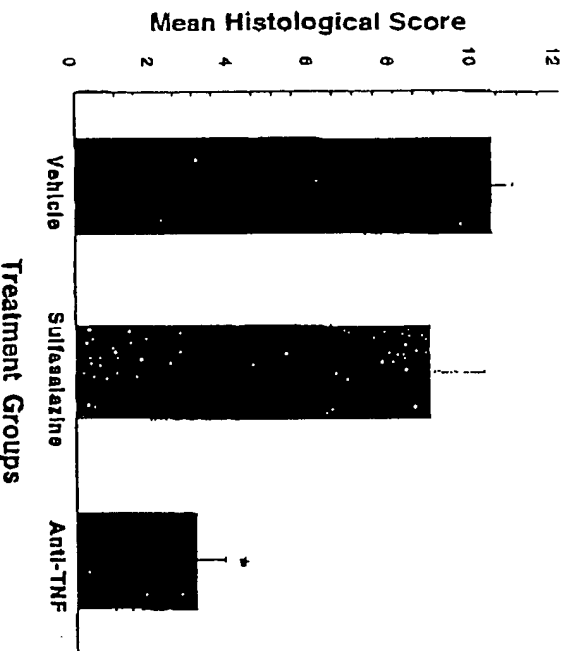Treatment Groups: Vehicle, Sulfasalazine, Anti-TNF

Figure 4.2. Oral administration of anti-TNF antibodies to rats 48 hours post treatment with TNBS significantly decreased morphological damage as compared to the vehicle control group (n=7, *p<0.002) and sulfasalazine group (n=7, p<0.005). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Sulfasalazine in the TNBS Animal Model

MPO (unit/gram/min.)
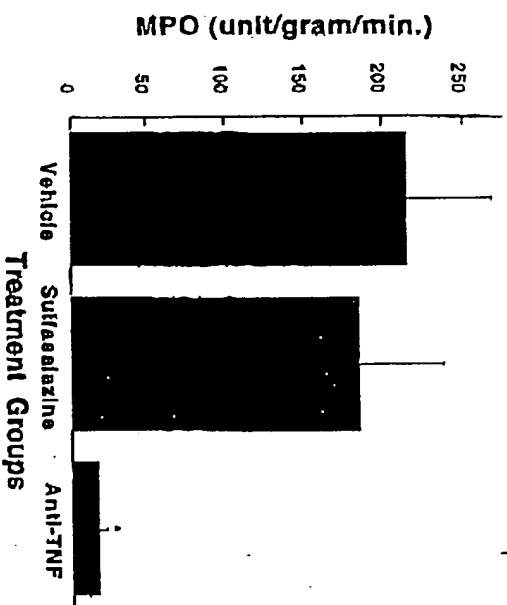

Treatment Groups: Vehicle, Sulfasalazine, Anti-TNF

Figure 4.4. Oral administration of anti-TNF antibodies to rats 48 hours post TNBS treatment significantly reduced the tissue myeloperoxidase as compared to vehicle (n=7, *p<0.002) and sulfasalazine (n=7, p<0.02). Mann-Whitney statistical test.

Figure 5

Treatment of Crohn's Disease by Anti-TNF is more Effective than Dexamethasone in the TNBS Animal Model

Total Colon Weight (grams)
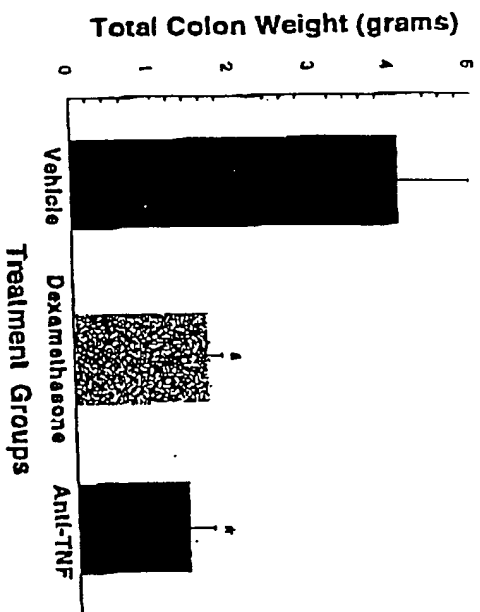
Treatment Groups: Vehicle, Dexamethasone, Anti-TNF

Figure 6.1. Oral administration of anti-TNF and dexamethasone significantly reduce total colon weight as compared to the vehicle control (n=8, *p<0.025 and p<0.05 respectively). Mann- Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Dexamethasone in the TNBS Animal Model

Histological Score

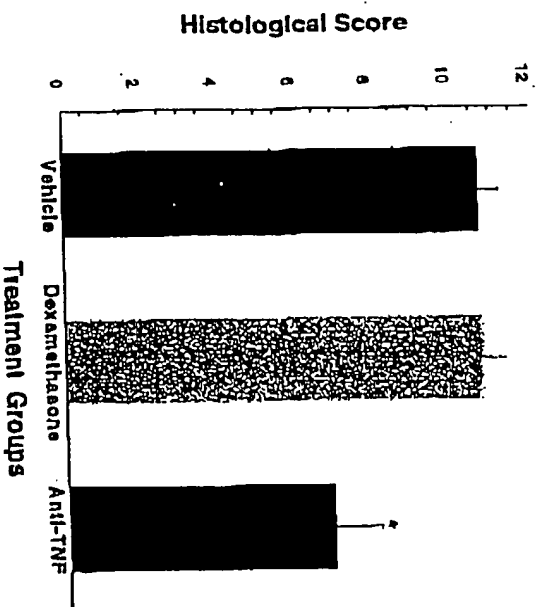Treatment Groups: Vehicle, Dexamethasone, Anti-TNF

Figure 6.3. Oral administration with anti-TNF significantly reduces histological damage as compared to the dexamethasone and vehicle treated animals (*n=9, p<0.001 and p<0.01). Mann- Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Dexamethasone in the TNBS Animal Model

Morphological Damage Score

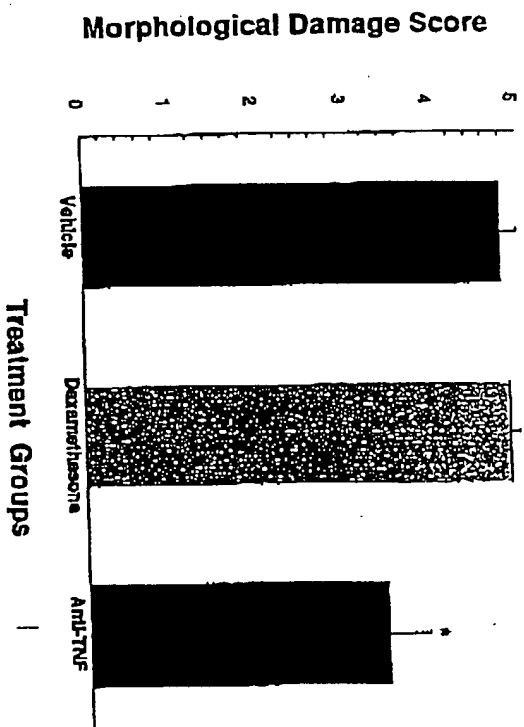Treatment Groups: Vehicle, Dexamethasone, Anti-TNF

Figure 5.2. Oral administration with anti-TNF significantly reduces morphological damage as compared to the vehicle and dexamethasone treated groups (*n=9, p<0.05 and p<0.025 respectively). Mann- Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF is more Effective than Dexamethasone in the TNBS Animal Model

MPO (unit/gram/min.)

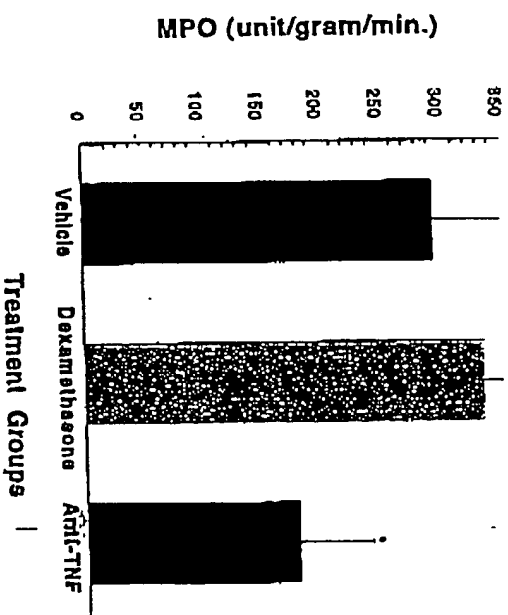Treatment Groups: Vehicle, Dexamethasone, Anti-TNF

Figure 5.4. Oral administration of anti-TNF significantly reduces myeloperoxidase levels as compared to dexamethasone treated animals (*n=9, p<0.05). Mann- Whitney statistical test.

Figure 6

in the Chronic TNBS Animal Model

Colon Weight (grams)
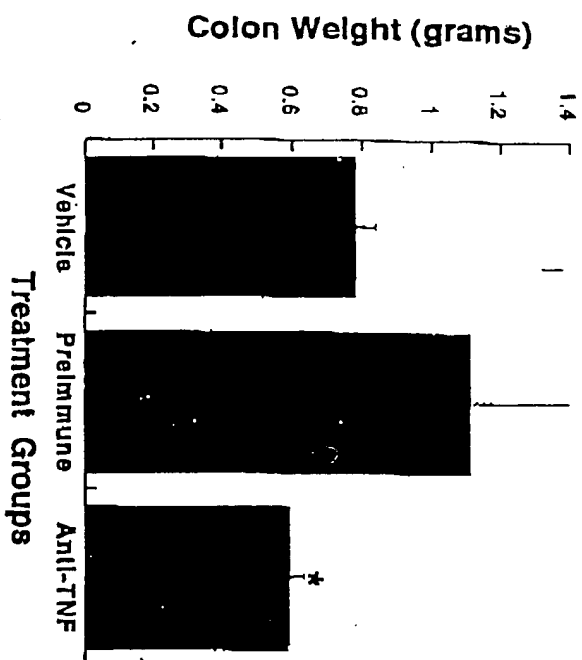

Treatment Groups

Vehicle   Preimmune   Anti-TNF

Figure 6.1. Oral treatment with anti-TNF significantly decreases the colon weight as compared to the vehicle and preimmune controls. (*p<0.025 Vs. vehicle and preimmune) Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF in the Chronic TNBS Animal Model

Morphological Damage Score
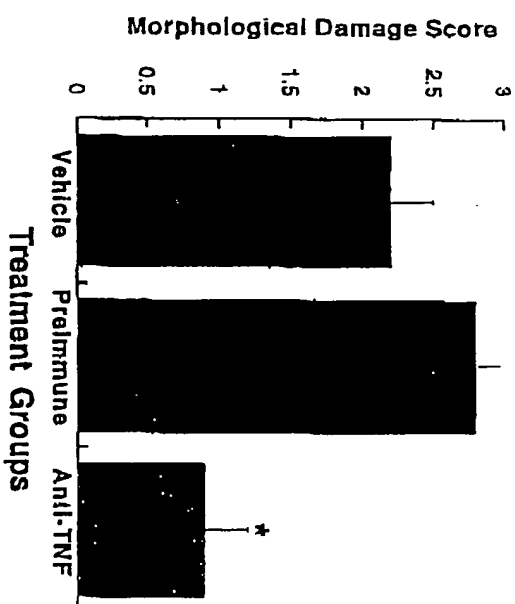

Treatment Groups

Vehicle   Preimmune   Anti-TNF

Figure 6.2. Oral treatment with anti-TNF significantly decreases morphological damage as compared to the vehicle and preimmune controls (*p<0.025 Vs. vehicle and preimmune). Mann-Whitney statistical test.

Treatment of Crohn's Disease by Anti-TNF in the Chronic TNBS Animal Model

Histology Score
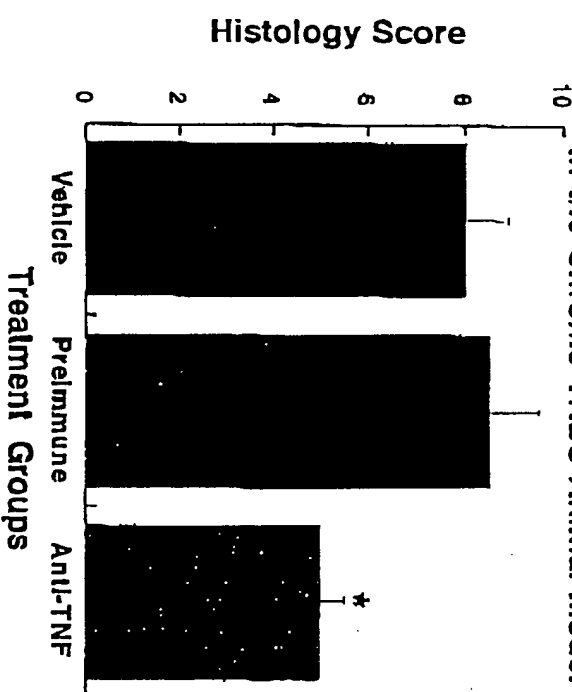

Treatment Groups

Vehicle   Preimmune   Anti-TNF

Figure 6.3. Oral treatment with anti-TNF significantly decreases the microscopic damage as compared to the vehicle and preimmune controls (p<0.025 and p<0.01 respectively). Mann-Whitney statistical test.

Figure 7

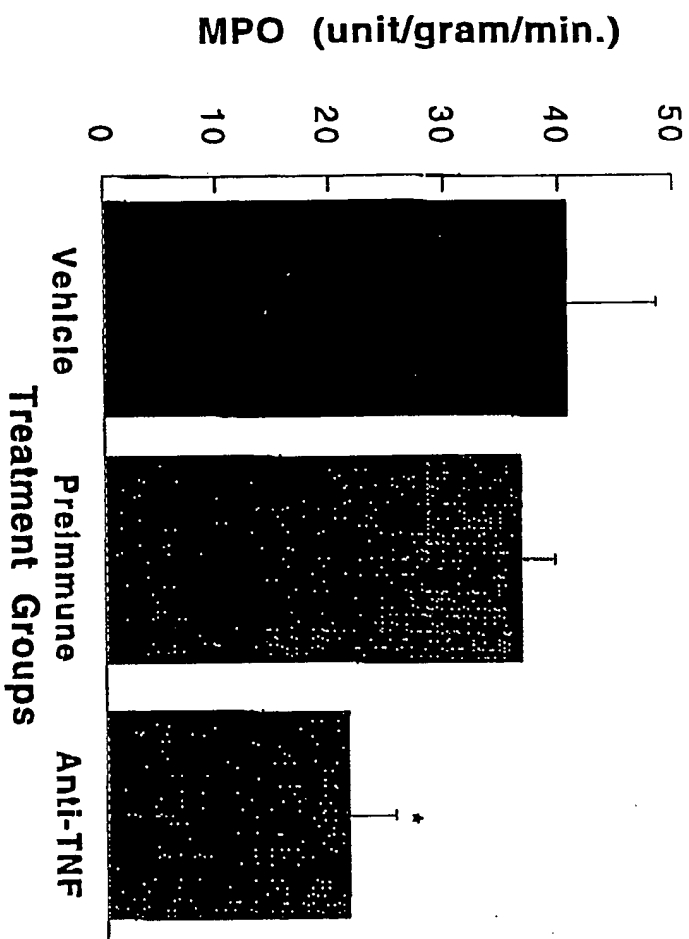## Treatment of Ulcerative Colitis by Anti-TNF in the DSS Animal Model

Figure 7.1. Intrarectal delivery of anti-TNF antibodies beginning day 3 of a 7 day DSS treatment regimen significantly reduces tissue myeloperoxidase levels as compared to preimmune control (n=5, *p<0.05), but not the vehicle control (n=10 , *p<0.2) Mann- Whitney statistical test.

Figure 8

Treatment of Ulcerative Colitis by Anti-TNF in the DSS Animal Model

Percent Positive Hemoccult
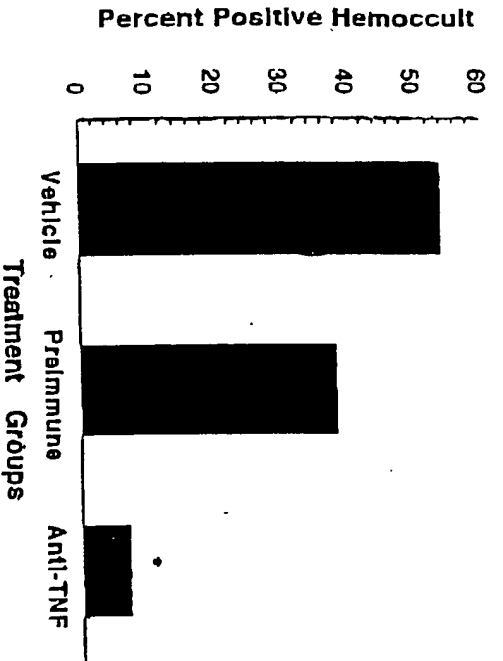
Treatment Groups: Vehicle, Preimmune, Anti-TNF

Figure 8.1. Intrarectal delivery with anti-TNF after 5 days of DSS treatment significantly reduced occult blood found in the stool of DSS treated mice as compared to the vehicle control. (*p<0.05) Chi-squared statistic

Treatment of Ulcerative Colitis by Anti-TNF in the DSS Animal Model

Histology Score (mean +/- SEM)

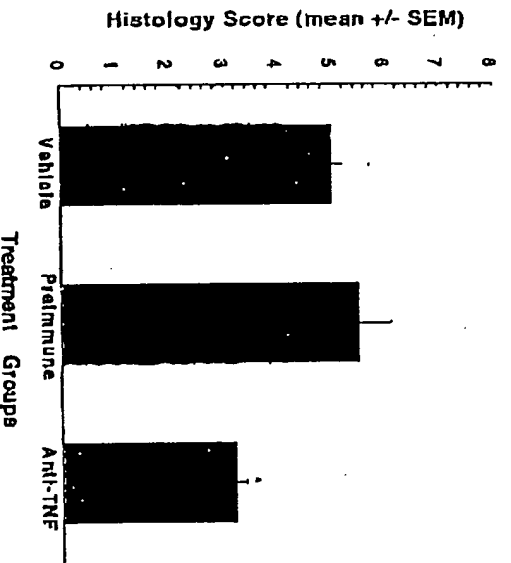Treatment Groups: Vehicle, Preimmune, Anti-TNF

Figure 8.2. Intrarectal treatment with anti-TNF antibodies after 5 days of DSS treatment significantly reduced histological damage as compared to vehicle control (*p<0.02) and preimmune controls (*p<0.01). Mann-Whitney statistical test.

Treatment of Ulcerative Colitis by Anti-TNF in the DSS Animal Model

MPO (units/gram/min)

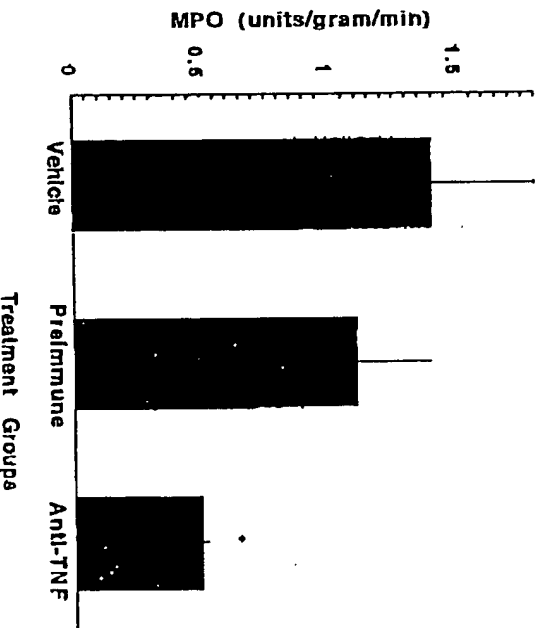Treatment Groups: Vehicle, Preimmune, Anti-TNF

Figure 8.3. Intrarectal delivery of anti-TNF antibodies after 5 days of DSS treatment decreased tissue myeloperoxidase levels as compared to the vehicle control (*p<0.05) and the preimmune control (*p<0.05). Mann-Whitney statistical test.

Preimmune   Anti-IL-6   Anti-IL-8   Anti-IL12

Treatment Groups

Figure 11.4. Oral treatment with anti-IL-6, 8, and 12 decreased the tissue MPO levels. Anti-IL-8 significantly lowered the MPO as compared to the preimmune control *(n=8, p=0.05).

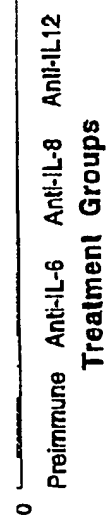Preimmune   Anti-IL-6   Anti-IL-8   Anti-IL12

Treatment Groups

Figure 11.3. Oral treatment with anti-IL-6, 8, and 12 decreased the histological damage from TNBS, as compared to the preimmune control. Only anti-IL-6 treatment was statistically significant *(n=6, p=0.05).

Figure 12

Acute Model of IBD: Weight Data

Weight (grams)

Days (Post Iniation of DSS treatment)

Pre-Immune
Anti-TNFalpha
Untreated